

Docket No 62661 (52171)  
(PATENT)

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Application of:  
Alexander Dömling et al.

Application No.: 10/520,793

Confirmation No.: 9957

Filed: July 09, 2003 (PCT/EP03/07419)

Art Unit: 1625

For: NOVEL TUBULYSIN ANALOGUES

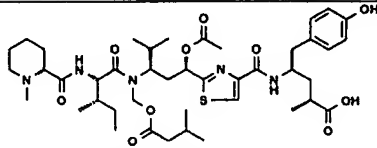
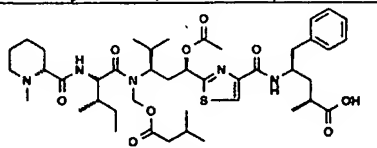
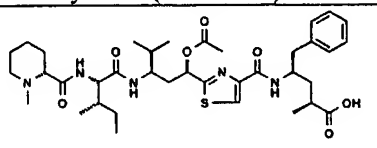
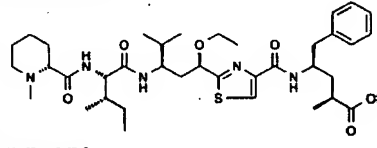
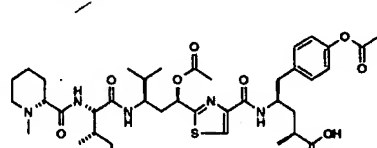
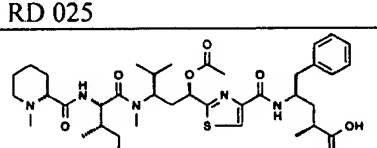
Examiner: Celia C. Chang

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

**DECLARATION OF WOLFGANG RICHTER, PH.D, UNDER 37 C.F.R. § 1.132**

I, Dr. Wolfgang Richter, declare as follows:

1. I am managing Director of R&D Biopharmaceuticals GmbH, Munich , Germany. My field of research and expertise is in the area of organic and medicinal chemistry.
2. The following experimental data was obtained in accordance with the following citations:  
T.-T. Yang, P. Sinai, S.R. Kain, Analytical Biochemistry **241**, 103-108 (1996);  
G. Kaur, M. Hollingshead, S. Holbeck, V. Schauer-Vukasinovic, R.F. Camalier, A. Dömling, S. Agarwal, Biochem. J. (2006) **396**, 235-242.
3. The following experimental data exemplifies that the derivatives with H or Me at the nitrogen left to the isopropyl group show a similar activity as the natural tubulysin A or D.

 Tubulysin A (Reference)	HT-29 [nM]  1.3-5.0		A2780 [nM]  1.7-2.1	KB-3-1 [ng/ml]  	L929 [ng/ml]  0.2
 Tubulysin D (Reference)				KB-3-1 [ng/ml]  0.07-0.8	L929 [ng/ml]  0.03
 Tubulysin U	HT-29 [nM]  3.8				L929 [ng/ml]  2.3
 RD 079		MCF-7 [ng/ml]  0.62			L929 [ng/ml]  3.4
 RD 025		MCF-7 [ng/ml]  2.4			L929 [ng/ml]  35
 RD 080	HT-29 [nM]  1.5				

4. According to the IC-50 data against different cancer cell lines it is clearly demonstrated that the derivatives with H or Me at the nitrogen left to the isopropyl group show a similar activity as the natural tubulysin A or D.

5. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and, that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful statements may jeopardize the validity of the application or any patent issued thereon.

Date: May 6<sup>th</sup>, 2009

Respectfully Submitted,

By: Wolfgang Richter